REMARKS

Claims 1-14, 17-23, 64, and 67-112 were pending in the instant application. By this amendment, claims 1-14, 17-23, 64, 67-79, 82, 93, 97-103 drawn to non-elected inventions, have been cancelled without prejudice to Applicants' right to pursue the cancelled inventions in this or other applications. Claims 85-87 and 89-92 were withdrawn from consideration by the Examiner as belonging to non-elected species. Since Applicants believe that the generic claim 80 is allowable, claims 85-87 and 89-92 should be considered by the Examiner and entered into prosecution upon allowability of the generic claim. Applicants respectfully request that these claims be considered by the Examiner.

Claims 88, 94, 104-106, and 109-112 have been amended. In particular, claims 88, 94, 104-106, and 109-112 have been amended to delete dependency from cancelled claim 93. Claim 107 has been cancelled because of redundancy with claim 88 and claim 108 has been amended to depend from claim 88.

Therefore, claims 80, 81, 83-92, 94-96 and 104-106, and 108-112 will be pending upon entry of the instant amendments in the instant application. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. THE OBJECTION TO CLAIMS 94, 104-107, AND 112 SHOULD BE WITHDRAWN

Claims 94, 104-107, and 112 have been objected to by the Examiner for certain informalities. In particular, claims 94 and 104-106 have been objected to because the claims recite a claim in the alternative that is drawn to a non-elected invention.

In response, claims 94 and 104-106 have been amended to delete dependency upon cancelled claim 93. These amendments have been made without prejudice to Applicants' rights to pursue the deleted subject matter in this or related applications. As noted above claim 107 has been cancelled because of redundancy with claim 88, thus the objection with respect to claim 107 have been obviated.

Claim 112 has been objected to because the claim recites sequences in the alternative, which the Examiner contends are drawn to non-elected inventions. Applicants submit that claim 112 recites species within the genus recited in claim 80, and thus all of the sequences recited in claim 112 should be considered by the Examiner upon allowability of the generic claim. Applicants respectfully request that these claims be considered by the Examiner.

In view of the amendments to the claims, Applicants respectfully request withdrawal of the objections to claims 94, 104-106, and 112.

2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 80, 81, 83, 84, 88, 94-96, and 104-111 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner contends that the specification lacks adequate written description support for the terms "ligand binding fragment of α2MR" and "small molecule."

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, pp. 1099-1111), specifies that an applicant may show that an invention is complete by "disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention." (*Id.* at page 1106, column 1, lines 22-33). According to the Guidelines, for each claimed genus, the test requires determination of whether there is sufficient description of

> " . . .a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus." *Id.* at page 1106, column 3, lines 12-29.

Where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced.

The Guidelines also state that "...when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus." In accordance with the written description guidelines, the disclosure of a single

species may provide an adequate written description of a genus when the species disclosed is representative of the genus.

Furthermore, in accord with the Written Description Guidelines, what is conventional or well known to one of skill in the art need not be disclosed in detail and where the level of knowledge and skill in the art is high a written description questions should not be raised (see Fed. Reg. Vol. 66, no. 4, January 5, 2001, p. 1106).

On page 4, ¶ 1, the Examiner states that "The written description in this case has only set forth the sequence of SEQ ID NO:7 which corresponds to full length human α2 macroglobulin receptor (herein α2MR), and therefore the written description is not commensurate in scope with the claims which read on ligand-binding fragment of α2MR." Contrary to the Examiner's statement, the specification describes an 80kDa ligand-binding fragment of α2MR (see page 12, lines 32-33, and Fig.8B). In example 6.3, the results at page 70 line 10 through page 71, line 6 demonstrate that the heat shock protein gp96 cross-links with the 80kDa ligand-binding fragment of α2MR derived from re-presentation competent cell types, thus indicating that the 80 kD fragment of α2MR binds to HSP. Moreover, the use of α2MR fragments of at least 5 consecutive amino acids of the sequence is taught in the specification (see page 7, lines 26-28).

HSP-binding fragments of α2MR are also described at page 52, lines 1-20. The specification also describes the functional domains of the α2MR, including the ligand binding portion of α2MR, at page 3, line 18 through page 4, line 13, page 12, lines 28-35, Fig. 8B, and Herz *et al.*, 1988, EMBO J. 7:4119-4127 and Horn *et al.*, 1997, J. Biol. Chem. 272:13608-13613 referenced therein (Information Disclosure Statement reference Nos: AZ and BD, respectively, previously submitted). In particular, the specification references Horn *et al.* as describing a portion of Cluster II of α2MR which contains complement repeats 3-10 (CR3-10), as a major ligand binding portion of the receptor (see page 3, lines 25 and 26). Thus, in addition to the example disclosed, the specification describes both the structure and function of α2MR fragments.

In the present instance, Applicants submit that disclosure of these species is sufficient to meet the written description requirement for ligand-binding fragments of α2MR. In particular, the 80kDa fragment and CR3-10 portion of α2MR are representative of ligand-binding fragments of α2MR. Thus, the disclosure of representative species combined with the structural and functional disclosure of binding domains α2MR is sufficient to meet the written description requirements.

With respect to small molecules, Applicants submit that the term "small

molecule" is conventional[1] and that the level of knowledge and skill in the art is high. As well known in the art, the term "small molecule" refers to a chemical compound having a molecular weight less than about 2500 amu. The compounds in the commercially available libraries of small molecules referenced in the specification are consistent with this standard meaning of "small molecule." Applicants also submit that sufficient examples of small molecules are provided in the specification to meet the standard for written description. For example, the specification provides examples of libraries of small molecules for use in the claimed methods that can be commercially obtained from Specs and BioSpecs B.V. (Rijswijk, The Netherlands), Chembridge Corporation (San Diego, CA), Contract Service Company (Dolgoprudny, Moscow Region, Russia), Comgenex USA Inc. (Princeton, NJ), Maybridge Chemicals Ltd. (Cornwall PL34 OHW, United Kingdom), and Asinex (Moscow, Russia) (see page 36, line 33 through page 37, line 13).[2] The specification also indicates that compounds can be small organic or inorganic molecules (see page 35, lines 17-18).

For all of the forgoing reasons and examples of small molecules, one skilled in the art would recognize that the Applicants were in possession of small molecules that can be used as test compounds in the claimed methods for identifying compounds that modulate an HSP-α2MR-mediated process. Thus, in accordance with the Written Description Guidelines, the term "small molecule" is sufficiently described and a written description rejection is improper.

In view of the forgoing arguments and amendments, Applicants respectfully request the Examiner's withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

[1] A search of the scientific literature published before year 2000 alone reveals more than 10,000 citations of the term lending further support to the proposition that the term is commonly used in scientific and pharmaceutical sciences parlance and would have been readily cognizable by a skilled artisan (see attached Exhibit A).

[2] Applicants will submit a Supplemental Response with portions of the relevant catalogs that exemplify small molecules available in libraries. The catalogs of small molecules can be requested from the web sites of the companies listed (e.g., http://www.maybridge.com, http://www.comgenex.com, http://www.specs.net, http://www.asinex.com, and http://www.chembridge.com).

CONCLUSION

Entry of the foregoing amendment and remarks into the record of the above-identified application is respectfully requested. Applicants submit that the remarks and amendments made herein now place the claims in condition for allowance. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: January 5, 2005

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Exhibit A

SUMMARY OF DIALOG SEARCH CONDUCTED 1/05/05

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S SMALL()MOLECULE OR SMALL MOLECULES AND PUBLICATION YEARS=1950->1999

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           3523     5: Biosis Previews®
           3242    73: EMBASE
            120   434: SciSearch®
            132    50: CAB Abstracts
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DETAIL of SEARCH

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S SMALL()MOLECULE OR SMALL()MOLECULES

Your SELECT statement is:
   S SMALL()MOLECULE OR SMALL()MOLECULES

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           1995   434: SciSearch®
            386    50: CAB Abstracts

   All files have one or more items; file list includes 5 files.

File 155: MEDLINE® PUBLICATION YEARS=1950->1999
       (c) format only 2005 The Dialog Corp.


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Exhibit A

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ADDITIONAL SEARCH
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